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LADAS & PARRY LLP
1040 Avenue of the Americas
NEW YORK, NY 10018-3738

EXAMINER	
POLANSKY, GREGG	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/651,305
Filing Date: August 28, 2003
Appellant(s): WANG, CHIA-GEE

Clifford J. Mass
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 11/12/2010 appealing from the Office action mailed 4/15/10.

(1) Real Party in Interest

The Examiner has no comment on the statement, or lack of statement, identifying by name the real party in interest in the brief.

(2) Related Appeals and Interferences

The Examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The following is a list of claims that are rejected and pending in the application:

1, 3, 5, 7, 12, 16-24, 26-36, 38, 40, 42, 51-59, 61-65, 67, 69, 71, 76-88, 90, 92, 97 and 99.

(4) Status of Amendments After Final

The Examiner has no comment on the appellant's statement of the status of amendments after final rejection contained in the brief.

(5) Summary of Claimed Subject Matter

The Examiner has no comment on the summary of claimed subject matter contained in the brief.

(6) Grounds of Rejection to be Reviewed on Appeal

The Examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the Examiner except for the grounds of rejection (if any) listed under the subheading "WITHDRAWN REJECTIONS." New grounds of rejection (if any) are provided under the subheading "NEW GROUNDS OF REJECTION."

(7) Claims Appendix

The Examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant's brief.

(**8) Evidence Relied Upon**

6,244,848	MILLS	5-2001
5,627,871	WANG	5-1997

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 5, 7, 12, 16-24, 26-36, 38, 40, 42, 47, 51-59, 61-65, 67, 69, 71, 76-88, 90, 92, 97, and 99 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mills (U.S. Patent No. 6,224,848), in view of Wang (U.S. Patent No. 5,627,871).

Mills teaches, *inter alia,* a method for eliciting tissue necrosis in treating cancer, by administering a compound (*e.g.*, cisplatin) that binds to targeted tissue DNA, wherein said compound comprises an atom (*e.g.*, platinum) that is excitable with radiation in a distinct narrow frequency band and energy level, **causing an Auger electron cascade** resulting in radiolysis of DNA. See Abstract and columns 108-110, claims 1, 5, and 9). Note that the compound, cis-diamminedichloroplatinum (II), taught by Mills in column 109, line 8, is the chemical name of cisplatin. Since cisplatin taught in the reference is the same as cisplatin recited by the instant invention, the properties of the elected compound (cisplatin) recited by the instant claims would also be encompassed by the cisplatin taught by Mills. For instance, the rate of physiological excretion of cisplatin and stability against dissociation of platinum from cisplatin during the time prior to complete excretion of cisplatin (*e.g.*, instant Claims 16 and 17 respectively) would be identical in both the reference and the instant invention. Similarly, the K- and L-absorption edge of platinum and the amount of Auger electrons released from the platinum in cisplatin and their effective range would be identical in the Mills reference and the instant claims.

The instant invention differs from the cited reference in that the cited reference does not teach the Applicant's preferred method of eliciting Auger electron cascade (*i.e.*, using line emission x-rays) from the selected element (*i.e.*, platinum). However, the

secondary reference, Wang, teaches the preferred line emission x-rays to be well known in the art. See column 10, lines 27-51. Wang teaches an end window transmission x-ray tube possessing a metal foil target on said end window, the thickness and composition of the metal foil target and the e-beam energy focused thereupon generate a micro-focused bright line x-ray beam of pre-selected energy. See Abstract.

Therefore, one skilled the art would have understood that the substitution of one monochromatic energy source (which causes an Auger electron cascade in the target metal, *e.g.*, platinum in cisplatin) for another monochromatic energy source capable of producing an Auger electron cascade in the metal. It would have been obvious to the artisan to use the x-ray source taught by Wang because of the increased convenience and logistics of using the smaller and more easily transported x-ray tube as opposed to the synchrotron taught by Mills.

The references do not teach the treatment of cells removed from and returned/transplanted back to a mammal. The references do not teach a kit comprising an x-ray tube having a target comprising a selected metal, and a compound (cisplatin) comprising a selected element (Pt).

On skilled in the art would have well versed in the practice of removing bone marrow and various other cells from the body for treating certain cancers (*e.g.*, x-ray treatment) and returning/transplanting these cell back into the body. It would have been obvious to use the methods taught by Mills and modified by the teachings of Wang to seek an improved cancer therapy. It would also have been obvious to said artisan to

"package" the essential components necessary to practice these methods. One would have been motivated to do so to provide a more convenient and efficient means for practicing a method of cancer therapeutics.

(10) Response to Argument

Appellant argues that Mills teaches a therapy that relies upon Mossbauer absorption as opposed to radiation with x-rays. As explained in the Wang Declaration, the emission and absorption of gamma-rays in a solid under the Mossbauer effect initiated by a nuclear decay is very different from the Auger cascade and the Auger dose initiated by a controlled external photon beam as claimed. In Mills, the nuclei of administered isotopes at the target tissue absorb gamma-rays and undergo an internal conversion, which is followed by an **Auger electron cascade** (see Mills at Abstract and claim 5). In the claimed invention, an **Auger cascade** commences when the atom, not the nucleus, has an inner shell ionization caused by K-edge or L-edge absorption initiated by a controlled external photon beam which leads to a number of low energy Auger electrons in a cascade whose kinetic energy is between 12-18 eV with a range of 5-10 atomic dimensions in water (Wang Declaration at paragraphs 4-7). Mills does not show or suggest the use of a controlled external irradiation source to induce a large radiation dose *in situ* next to a target atom. [Emphasis added]

The Examiner respectfully disagrees. Appellant acknowledges that Mills teaches the use of an energy source to precipitate an Auger electron cascade from the same instantly claimed target elements. Appellant is arguing that Mills teaches the

precipitation of the Auger electron cascade by internal conversion of gamma-ray energy absorbed by the target element nucleus to release energy to precipitate an Auger electron cascade, as opposed to the instant invention's x-ray energy acting on the target element electron shells to precipitate the same Auger electron cascade. As discussed in the rejection of record, Mills teaches an Auger electron cascade is responsible for the therapeutic (*i.e.*, tumor-cell destruction) effects of the disclosed method. Although Mills teaches the use of a finely controlled gamma-ray source instead of the instantly claimed controlled x-ray source for the initiation of an Auger electron cascade from the selected element (e.g., platinum) associated with the DNA of the target cells, the reference none-the-less teaches the mechanism for destroying the target cells is the same: an emission of Auger electrons from the selected element associated with DNA of the irradiated cells causing the selective and localized destruction of the target cell. There is no difference in the energy of the Auger electrons precipitated by the gamma-ray source of Mills or the x-ray source instantly claimed; the therapeutic effect is, therefore, also the same.

Appellant argues that "[o]ne of ordinary skill in the art would have had no reason or motivation to substitute the claimed line emission x-rays for the gamma-rays of Mills. To the contrary, the principle of operation described in Mills is tied to 'a radiation source which provides energy at the corresponding resonant Mossbauer absorption frequency of isotope containing pharmaceutical'".

The Examiner respectfully disagrees. The use of x-rays or gamma-rays in the treatment of tumors is well known in the art (Mills, column 1, lines 23-24). One of ordinary skill would have recognized that an Auger electron cascade can be precipitated

by means other than described by Mills (e.g., x-rays instead of gamma-rays). The reference to Wang teaches an Auger electron cascade precipitated by an x-ray source which reads on the x-ray source of the instant claims (e.g., column 10, lines 27-51). The method of eliciting an Auger electron cascade using x-rays taught by Wang offers improved convenience and logistics of using the smaller and more easily transported x-ray tube as opposed to the synchrotron taught by Mills. Further, the x-ray source of Wang provides "a desired x-ray flux with a minimum of white x-ray radiation. Such a mode of x-ray generation more resembles a synchrotron wiggler than a traditional x-ray tube." See Wang, column 9, lines 24-28. The K- and L-absorption edge of platinum and the amount of Auger electrons released from the platinum in cisplatin and their effective range would be identical in the Mills reference and the instant claims. Further, in the 6/02/2008 response to the Office action of 11/29/2007, Appellant argued that the K-absorption and L-absorption edge for platinum "were well known to those of skill in the art as of the application filing date." See lines 7-8 of the 5th page (labeled page 22) of Appellant's Remarks, filed 6/02/2008. This provides further evidence that one skilled in the art at the time of the invention would have known the amount of energy needed from the x-ray source of Wang to precipitate an Auger cascade from inner shell ionization caused by K-edge or L-edge absorption of the external energy.

Appellant argues:

> Mills would not have provided even a reasonable expectation of success with the claimed method since one of ordinary skill in the art could not have expected that the use of **external x-rays** generating the claimed dose of 10^6 Gy *in situ* could be made without unacceptable damage to a

patient. Indeed, prior art patents dealing with radiosurgery from an external x-ray source teach away from this. For example, Cash et al US Patent 6,366,801 describes radiosurgery with the use of a heavy element contrast agent in connection with a monochromatic x-ray source with distinct and specific frequency and energy level properties (see Cash at column 8, line 46 to column 9, line 39 ('Optimized X- ray Spectrum')). Cash teaches that it is necessary to limit the radiation to a dose that is orders of magnitude less than the claimed dosage of 10^6 Gy *in situ*. See Cash et al at, e.g., column 12, lines 43-48 ('a preferred approach is to irradiate the patient 10 so that the tumor receives 1600 cGy in a single dose, and the surrounding healthy tissue receives 1600/de cGy.'); see, also, Cash at column 15, Example 1 ('At the skin, a dose of 10 Gy accumulates, which is **too high for healthy skin**.' Emphasis added.).

The Examiner disagrees. The instant invention is drawn to the administration of external x-rays having sufficient energy to precipitate an Auger electron cascade (from a pre-selected element (e.g. platinum) in the administered compound), in a dose effective to disrupt DNA proximate to the irradiated pre-selected element. It is claimed that the Auger electrons administer a dose of at least 10^6 Gy localized within a few atomic diameters from the pre-selected element. The external x-ray source is **not** directly irradiating the subject with 10^6 Gy as Appellant seems to be suggesting. The 10^6 Gy dose of the instant claims is that which is precipitated by the Auger electrons of the target metal over a very short distance, which is what is taught by Mills. One of ordinary skill, as discussed above, would have modified Mills by the substitution of another energy source (the x-ray tube of Wang) to precipitate the Auger electron cascade, which would naturally administer the same dose to the target cells as is instantly claimed.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the Examiner in the Related Appeals and Interferences section of this Examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Gregg Polansky/

Examiner, Art Unit 1629

Conferees:

/James D Anderson/

Primary Examiner, Art Unit 1629

/Jeffrey S. Lundgren/

Supervisory Patent Examiner, Art Unit 1629

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627